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EXAMINER

BRUMBACK, B

ART UNIT	PAPER NUMBER
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1642

DATE MAILED:

06/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
08/591,651

Applicant(s)

Classen

Examiner
Brenda Brumback

Group Art Unit
1642



☒ Responsive to communication(s) filed on May 1, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55 are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55-101 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

1. Appellant's Brief filed 05/01/2000 has been entered as Paper # 24. Upon further review and consideration of the record, prosecution is hereby reopened in order to expand the rejections.
2. Pending claims are 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55-101. Claims 6, 32, 33, 56-58, and 101 are drawn to methods; claims 5, 8, 10, 11, 15, 16, 26-30, 34-41, 43, 44, 46, 48-52, 55, and 59-100 are drawn to kits. Claim 19 is drawn to an immunogenic agent.
3. All outstanding rejections of claims under 35 U.S.C. 112 are hereby withdrawn in light of the new grounds of rejection under 35 U.S.C. 112, first and second paragraphs, which follow.

NEW GROUNDS OF REJECTION

Claim Objections

4. Claims 5, 6, 19, 30, 32, 37, 56-58, 67, 69-71, 73, and 75- 77 are objected to because of the following informalities:

The nomenclature used to recite the immunogens in the present claims is inconsistent. All claims should either be amended to recite the immunogen by the name of the etiologic agent, or by adding the term "vaccines" after the listing of disease names. Furthermore, bacterial names are

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conventionally written listing genus and species either in italics or underlined with the genus name capitalized. Also, the complete virus names of the viral immunogens should be recited. For example, "varicella" should be amended to varicella-zoster virus. Finally, all claims should be reviewed for punctuation, as commas are absent between some of the immunogens (see claim 19, line 11, "dengue toxoplasmosis" for example).

In claim 35, line 3, and in claim 85, line 2, "erythematosus" is misspelled.

Claim 37 is objected to for an informality in grammar. The syntax is incorrect.

Claim Rejections - 35 USC § 112

5. Claims 5, 6, 8-11, 15, 16, 19, 26-30, 34-57, 77, and 86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is indefinite as lacking clear antecedent basis. Claim 6 recites "wherein for at least one such immunogen, the total dosage during the first 112 days after birth...". Claims 6 depends from claim 32, which recites dosages during the first month or prior to 42 days after birth, not 112 days. Claim 57 is also indefinite for the same reason; claim 57 depends from claim 56, which also recites dosages during the first month or prior to 42 days after birth.

Claim 6 is also indefinite for recitation of a total dosage which is "substantially" greater than that required for immunization against an infectious disease. The disclosure fails to teach

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how much is “substantially” more; thus the metes and bounds of the claimed invention cannot be determined.

Claims 11 and 38 are indefinite as lacking clear antecedent basis. Claims 11 and 38 recite instructions pertaining to the first 175 or 112 days from birth. Claim 11 and 38 depend from claim 59. The instructions recited in claim 59 do not pertain to the either first 175 or the first 112 days after birth.

Claim 19 is indefinite for recitation of immunogens by the disease name, rather than by the name of the etiologic agent, for those diseases which may be caused by any of a plurality of agents, such as encephalitis and pneumonia, for example. Claim 19 is also indefinite for recitation of “herpes” without delineating which of the herpesviruses is the immunogen; “herpes” can refer to herpes simplex virus; other human herpesviruses, such as human herpesvirus 6 for example; as well as a myriad of animal herpesviruses. Finally, claim 19 is indefinite for recitation of “a molecule that cross reacts immunologically to at least one of said immunogens”. The specification fails to teach the metes and bounds of such a molecule having immunological cross reactivity. Is it intended to be a molecule which elicits a protective immune response to the antigen with which it cross reacts, or is it intended to be a molecule which cross-reacts with the immunogen in an immunoassay?

Claim 27 is indefinite for recitation of “acting to substantially reduce the incidence...”. The disclosure fails to teach how much is “substantially” and one would not be apprised of the metes and bounds of the claimed invention.

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Claim 40 is indefinite for recitation of "the shortest interval" as "less than 28 days". "Less than 28 days" does not define a lower limitation of an interval. It is therefore unclear what interval is intended in the claimed invention.

Claim 48 recites a mammal which is an animal model of diabetes or systemic lupus erythematosus. The specific mammals encompassed with such an animal model are not clear.

Claim 77 is indefinite for being in improper Markush format. The Office recommends the use of the phrase "selected from the group consisting of..." with the use of the conjunction "and" rather than "or" in listing the species. See MPEP 706.03(Y).

6. Claims 5, 6, 8-11, 16, 30, 32, 38, 49, 55-65, 72, 74-101 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

A review of the record indicates that in applicant's amendment filed 03/25/1999 (Paper # 10), applicant amended claim 32 to introduce the additional limitations "where, if only one immunogen is administered according to said immunization schedule, that immunogen is one other than BCG" and "if said one immunogen is whole cell pertussis, the schedule is one other than a schedule of three doses at one week intervals, all given in the first month". Applicant also added new claim 56 incorporating the same limitations. Applicant indicated that support for the first limitation could be found from another patent which issued on the parent application and that

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support for the second amendment could be found in an article cited in the specification (see Paper # 10, page 11, first and second paragraphs). Matter not in the originally presented specification, claims, or drawings of the present application, is normally considered to be new matter (see MPEP 608.04(a)). It is thus unclear how applicant intends to rely upon an issued patent from a parent case or upon cited literature, rather than the specification, to provide support for amendments to the claims in the present application.

In the same amendment, applicant added new claim 58 reciting "where one or more immunogens are administered on at least four different dates during the first 42 days after birth". Applicant indicated (page 11, third paragraph, of Paper # 10) that support for this limitation could be found at page 27, lines 12-14, of the specification, in conjunction with schedule 1 on page 107. The examiner does not find support for the amendment as indicated. Applicant's specification discloses two or three doses within the first 42 days of birth at page 27 (see lines 12-14), not at least four. Schedule 1 at page 107 does not disclose any schedule of immunization by days after birth, but rather discloses weeks. Further clarification or cancellation of the newly recited material is required.

Additionally, in paper # 10, new claim 59 was added with the limitation (b) that the labeling or instructions in the kit indicate that the kit, depending on when one or more of the immunogens is administered, may, can, or does increase the incidence of accelerate the onset of a chronic immune-mediated disorder. Applicant indicated that support for this material could be found at pages 53-69 (see page 12, first sentence, of paper # 10). Upon review of the disclosure,

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the examiner does not find support for the claimed labeling or instructions. This matter might be resolved if applicant were to point out specifically where support for the newly recited material can be found.

Applicant also added new claim 89 in paper # 10 reciting an aluminum salt or "another adjuvant whose ability to activate macrophage is about the same as or greater than that of an aluminum salt". The examiner also does not find support for this material at page 75, lines 13-23, of the disclosure, as was indicated by applicant (see page 12 of paper # 10). Further clarification or amendment or cancellation of the claim is required.

7. Claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55-101 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the

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art” (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that “... where a statement is, on its face, contrary to generally accepted scientific principles”, a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to methods of reducing the incidence or severity of a chronic immune-mediated disorder in a mammal comprising administering one or more immunogens using specified dosage schedules at specific times after birth. The claimed immunogens are any of a specified group of live or killed viral, bacterial, and parasitic pediatric and non-pediatric immunogens (including BCG, tetanus, pertussis, rubella, *Haemophilus influenza* B [Hib], poliovirus, hepatitis B, and mumps, among others); the claimed chronic immune-mediated disorder is selected from diabetes and systemic lupus erythematosus,

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among others; and the mammal is a human or an animal model of diabetes. The claimed invention is also drawn to kits for which the intended use is to carry out the claimed methods; thus, the kit claims are rejected herein together with the method claims.

The state of the prior art and the predictability or lack thereof in the art: The Pediatric Infectious Diseases Journal, 1999;18:217-22; hereinafter PIDJ teaches that both genetic and environmental factors are associated with an increased risk of developing diabetes (see page 217, column 2, second full paragraph). The PIDJ teaches that available data are inconclusive with regard to a protective effect of vaccines against development of diabetes (see page 219, column 1, first full paragraph). PIDJ teaches that a study conducted in Sweden “revealed that children with type 1 diabetes were less likely to have received measles vaccination than comparable children without diabetes, but no association was noted for BCG, smallpox, tetanus, pertussis, rubella, or mumps” (immunogens which overlap the immunogens of the claimed invention). PIDJ also teaches that data regarding the marked variability in the incidence of type 1 diabetes within China also indicates that BCG does not affect the incidence of diabetes (see page 219, column 1, first full paragraph). PIDJ further teaches that “Because the incidence of type 1 diabetes mellitus has increased in countries with and without introductions of new vaccines into the immunization schedule, the data do not support the hypothesis that vaccines effect the risk of diabetes mellitus” (see the sentence bridging pages 219 and 220). Finally, PIDJ teaches that in a study of children at high risk for developing diabetes mellitus, “The timing and number of doses of polio, DPT, Hib or

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measles, mumps, and rubella vaccines were no different between case and control groups (see page 220, first full paragraph).

Boumpas et al. (Annals of Internal Medicine, 123(1):42-53) teach that the underlying pathogenesis of systemic lupus erythematosus (SLE) is unknown “despite intensive efforts to elucidate” it and that many genetic and environmental factors probably contribute to the disease. Boumpas et al. also teach that the autoimmune response in patients with SLE is extremely diverse among different patients. Boumpas et al. teach that treatment for SLE consists of various protocols for disease management according to the clinical manifestations, none of which incorporate vaccinations. Finally, Boumpas et al. teach “It is likely that different pathogenetic and etiologic disease-inducing factors operate in different patients, accounting for the marked heterogeneity in clinical and laboratory abnormalities seen in patients ...” (see the entire document and especially the paragraph bridging pages 50 and 51). Thus, Boumpas et al. teach that the etiology, pathogenesis, and clinical course of SLE is largely unknown, extremely complex, and different in different patients.

The amount of direction or guidance present and the presence or absence of working examples: In light of the teachings found in the prior art regarding the unpredictability of treating diabetes with vaccinations and the varied and largely unknown mechanisms of pathogenesis of SLE, detailed teachings are required in the specification in order to enable the skilled artisan to practice the invention as claimed, which is drawn to treating chronic immune-mediated disorders, such as diabetes and SLE, by administration of vaccines according to

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specified schedules. Such teachings are absent from the present disclosure. The disclosure teaches immunization of non-obese diabetic prone mice and diabetic prone BB rats as animal models for methods of treating diabetes in human (see Examples 1,2, and 3 beginning on pages 82, 83, and 85 respectively) and teaches that vaccination according to a specified schedule is preventative of the onset of diabetes in mice and rats. However, PIDJ teaches that selective vaccines are protective against type 1 diabetes in mice, but not in humans, *i.e.*, that the data generated from studies conducted using animal models is inconclusive in humans (see page 217, first column, third paragraph and page 218, the paragraph bridging columns 1 and 2). The disclosure also teaches analysis of retrospective immunization data as indicative of the efficacy of the claimed treatment methods (see pages 89-106). However, PIDJ teaches that "Ecologic studies may be used to generate hypotheses regarding possible factors associated with disease, but ecologic studies do not demonstrate causal relationships" (see page 219, the sentence bridging columns 1 and 2).

The disclosure contains the general teaching that the immunization protocols described for the diabetes animal models may also be used for mediating the onset and/or severity of other autoimmune diseases, such as SLE, among others (see the paragraph bridging pages 21 and 22, for example). However, the disclosure is completely silent as to if and how the immunization protocols for the diabetes models are to be adapted for other autoimmune diseases. There are no working examples of any animal models or epidemiological data regarding any autoimmune disease other than diabetes.

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The breadth of the claims and the quantity of experimentation needed: The claims are drawn to methods and kits for reducing the incidence or severity of chronic immune-mediated disorders comprising vaccination. The prior art does not teach vaccination as a means of treatment or therapy for any immune-mediated disorders other than diabetes. The prior art teaches that vaccination protocols have not been shown to have any significant effect in ameliorating the onset or severity of diabetes in humans. As outlined herein, the present disclosure fails to provide teachings which are sufficient to overcome the teachings of the prior art. For these reasons, it would require undue experimentation by the skilled artisan in order to be able to practice the claimed invention.

Claim Rejections - 35 USC § 101/ Double Patenting

8. Claims 2-17, 19, 21, 23-33, 34-55, 56-58, and 101 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-42 of Classen U.S. Patent No. 5,728,385 and claims 1-47 of Classen U.S. Patent No. 5,723,283 for the reasons of record. Applicant has made a statement of intention to either cancel the method claims or to file a terminal disclaimer upon indication of allowable kit claims.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

a. Claims 5, 8, 10, 11, 15, 16, 26-30, 34-41, 43, 44, 46, 48-52, 55, and 59-100 are drawn to kits comprising one or more immunogens with labeling indicating a specified immunization schedule for administration of the immunogens in order to reduce the incidence or severity of a chronic immune-mediated disorder.

b. Claims 8, 10, 11, 15, 16, 19, 26-30, 34-41, 43, 44, 46, 48-52, and 55 stand rejected under 34 U.S.C. 102(b) as being anticipated by Madore et al. (of record in Paper # 7). Claims 59-67, 72, 73, 76-77, 79, 89, 90, 92, 9, and 96-100 are also rejected under 34 U.S.C. 102(b) as being anticipated by Madore et al. Madore et al. teach a vaccination kit comprising an Hib immunogen and administration of the immunogen according to a defined dosage schedule in order to elicit antibodies against Hib (see the abstract).

c. Claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, and 46-52 stand rejected under 35 U.S.C. 102(b) as anticipated by Dengrove et al. (of record in paper # 7). Claims 59-67, 70-73, 76, 78, 79, 90, 92, 93, and 96-100 are also rejected under 35 U.S.C. 102(b) as being anticipated by Dengrove et al. Dengrove et al. teach vaccine kits comprising diphtheria and tetanus toxoid immunogens and teach administration of the immunogens according to a defined dosage schedule in order to elicit antibodies against diphtheria and tetanus (see the abstract).

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d. Claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, and 46-52 stand rejected under 35 U.S.C. 102(b) as anticipated by Halsey et al. (of record in paper # 7). Claims 59-67, 70-73, 76, 78, 79, 90-93, and 96-100 are also rejected under 35 U.S.C. 102(b) as anticipated by Halsey et al. Halsey et al. teach vaccination kits and immunogens comprising DPT and poliovirus immunogens and teach administration of the immunogens according to a defined dosage schedule in order to elicit antibodies.

e. Claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, and 46-52 stand rejected under 35 U.S.C. 102(b) as anticipated by John. New claims 60-67, 70, 72, 73, 78, 79, 90, 91, and 96-100 are also rejected under 35 U.S.C. 102(b) as anticipated by John. John teaches vaccine kits comprising poliovirus immunogens and teaches administration of the immunogens according to a defined dosage schedule in order to elicit antibodies.

New Grounds of Rejection:

f. Claims 5, 8, 10, 11, 15, 16, 19, 26-30, 34-41, 43, 44, 46, 48-52, 55, and 59-100 are rejected under 35 U.S.C. 102(b) as being anticipated by Benveniste and Lagrange et al., pp. 346-364 and 465-502 in Immunology, Bach et al., ed., John Wiley & Sons, New York, 1982). Bach et al. teach a variety of antigens which elicit an immune response and which encompass various yeast, mold, insect, and animal antigens (see page 351, first full paragraph). Lagrange et al. teach a variety of vaccines comprising bacterial or viral immunogens which overlap those of the claimed invention (see page 497, Table 16.5).

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While the labelling of the immunogens taught by any of Madore et al., Dengrove et al., Halsey et al., John, or Benveniste and Lagrange et al. is not the same as that in the claimed kits, applicant's labelling constitutes printed matter and as such is not given patentable weight over the kits and immunogens taught in the prior art, absent some functional relationship between the immunogens and the label or printed matter.

Response to Arguments

10. Applicant's arguments presented in the Appellant's Brief filed 05/01/2000 will be addressed to the extent that they pertain to the outstanding prior art rejections of the kit claims. Applicant has argued and continues to argue that there is a functional relationship between the printed matter or labeling in the claimed kits and the immunogen. Applicant's arguments have been fully considered and have been previously addressed at length; they are not persuasive because applicant has not demonstrated the existence of such a functional relationship. The immunogens of the claimed kits remain functional absent the labeling; therefore no functional relationship exists between the labeling and the immunogens that would be given patentable weight. In re Miller and In re Gulak relate to a mathematical device and to a measuring cup respectively. In each of these cases, the function of the device depends upon the printed matter itself which is a part of the substrate; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instant kits. The immunogens remain fully functional absent the labeling or printed instructions for use.

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Applicant also argues that the PTO has allowed claims with labelling limitations previously (see page 12 of the Brief). Such arguments are not persuasive because it is not clear how patents to such inventions as a drug dosage identification card, a drinking vessel, and a prescription drug package are relevant to the present rejection. Applicant is also reminded that patentability of an invention is determined on a case by case basis based on the statutes and relevant case law.

Conclusion

11. No claims are allowed,

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Anthony Caputa whose telephone number is (703) 308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1642 FAX telephone number is (703)-305-3014. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

Brenda Brumback
June 9, 2000


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